## (19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 30 June 2005 (30.06.2005)

**PCT** 

## (10) International Publication Number WO 2005/058915 A1



(51) International Patent Classification<sup>7</sup>: C07D 513/06, A61K 31/554, A61P 25/28 // (C07D 513/06, 281:00, 209:00)

(21) International Application Number:

PCT/EP2004/014076

(22) International Filing Date: 9 December 2004 (09.12.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 0328900.6

12 December 2003 (12.12.2003) GB

(71) Applicant (for all designated States except US): GLAXO GROUP LIMITED [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): REDSHAW, Saliy [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). DEMONT, Emmanuel, Hubert [FR/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). WALTER, Daryl, Simon [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB).

(74) Agent: GIBSON, Mark; GlaxoSmithKline, Corporate Intellectual Property (CN925.1), 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

## Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: TRICYCLIC INDOLE HYDROXYETHYLAMINE DERIVATIVES AND THEIR USE IN THE TREATMENT OF ALZHEIMER'S DISEASE

$$(R^{1})_{m} \xrightarrow{B} A \qquad (I)$$

$$(R^{2})_{n} \qquad (I)$$

(57) Abstract: The present invention relates to novel hydroxyethylamine compounds having Asp2 ( $\beta$ -secretase, BACE1 or Memapsin) inhibitory activity of formula (I), processes for their preparation, to compositions containing them and to their use in the treatment of diseases characterised by elevated  $\beta$ -amyloid levels or  $\beta$ -amyloid deposits, particularly Alzheimer's disease. Formula (I) wherein, inter alia, A-B represents -NR<sup>5</sup>-SO<sub>2</sub>- or -NR<sup>5</sup>-CO-; R<sup>5</sup> represents

hydrogen,  $C_{1-6}$ alkyl,  $C_{3-6}$  alkenyl,  $C_{3-6}$  alkynyl,  $C_{3-10}$  cycloalkyl,  $-C_{0-6}$  alkylaryl,  $-C_{0-6}$  alkyl-heteroaryl,  $-C_{0-6}$  alkyl-heteroaryl,  $-C_{3-10}$  cycloalkyl-heteroaryl; -W- represents  $-CH_{2^-}$ ,  $-(CH_2)_2$ -,  $-(CH_2)_3$ -, -C(H)=-C(H)- or  $-CH_2$ --C(H)=-C(H)-; -C(H)--C

) 2005/058915 A1